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Creatine Kinase Elevations in Marathon Runners: Relationship to Training and Competition

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Elevation of creatine kinase (CK) in serum after exertion is a reliable marker of skeletal muscle injury. Limited data exist on CK levels in conditioned athletes after endurance training and competition. Serum CK was measured by a kinetic UV method (normal < 100 U/L) in 15 long distance runners before (pre-race), 24 hours after (post-race$_1$) and four weeks following (post-race$_2$) the 1979 Boston Marathon. CK levels were elevated throughout the study. Mean values for all runners and for those finishing before and after three hours and 30 minutes are as follows:

	Pre-Race	*Post-Race*$_1$	*Post-Race*$_2$
15 Runners	161 (U/L)	3424	157
Under 3:30 (10)	173 (U/L)	4433	166
Over 3:30 (5)	130 (U/L)	1432	135

Post-race$_1$ CK was significantly elevated among the ten faster as compared to the five slower runners ($p = 0.025$). Elevations of creatine kinase drawn 24 hours post-marathon are inversely related to finishing times among the runners tested.

INTRODUCTION

Increased activity of creatine kinase (CK) may occur in serum in healthy subjects after exercise and serves as a marker of injury to skeletal muscle [1-2]. A spectrum exists from fulminant rhabdomyolysis as reported in military recruits [3] to asymptomatic elevations in recreational athletes after exercise [4], where the degree of biochemical abnormality reflects the extent of tissue injury. The risk of rhabdomyolysis has been related to the adequacy of physical conditioning of subjects for the exertion performed and to the duration and intensity of exercise. Limited data exist on creatine kinase levels in specifically conditioned athletes such as long distance runners during training and after competition.

To determine these relationships, creatine kinase was assayed by a kinetic UV method (normal <100 U/L) in a group of male marathon runners before and sequentially after the 1979 Boston Marathon. Mean values were elevated before (161 U/L), peaked 24 hours after (3424 U/L), and returned to pre-race levels four weeks

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after (157 U/L) the marathon. The marked elevation of CK within 24 hours after competition indicates substantial if transient rhabdomyolysis, while lesser elevations occur during training.

To assess the relationship of these elevations to conditioning, CK values were analyzed by the finishing times of participants. Using three hours and 30 minutes as a dividing point, mean CK in the post-race$_1$ samples was 4433 U/L among the ten faster and 1432 U/L among the five slower runners, which is statistically significant ($p = 0.025$). This inverse correlation between enzyme elevations and finishing times deserves further study.

SUBJECTS, MATERIALS, AND METHODS

The study population consisted of 15 male long distance runners who competed in the eighty-third running of the Boston Marathon on April 16, 1979. Nine runners were officially qualified entrants by standards of the Boston Athletic Association in force at the time (<3 hours for males under age 40, <3½ hours for males over age 40), while six were registrants in the Doctors' Marathon sponsored simultaneously by the American Medical Joggers Association with endorsement of the BAA. After appropriate informed consent, data were obtained from each participant on extent of training and prior marathon running experience. The relevant characteristics of runners as a group and by category of registration are shown in Table 1. The mean ages were comparable between the BAA-qualified and AMJA-registered runners, although the former reported two times the number of training miles per week and prior marathons run as did the latter. All runners completed the official distance of 42.195 kilometers without injury or medical complications, and accurate finishing times were available for each participant.

Blood samples were obtained from each runner before, 24 hours after, and four weeks following the race. The time course of peaks in serum CK had been previously determined by one of us (LS, unpublished data) and was verified among a subset of runners in this study. All 15 runners were tested at four weeks, at which time CK activity had returned to a pre-race level and most runners had resumed their customary training.

All sera were frozen and stored at -20° Centigrade until the time of enzyme analysis. Creatine kinase was assayed by a kinetic UV method monitored at 340 nm, employing a KA-150 enzyme analyzer (Perkin-Elmer, Norwalk, CT) using STAT-PACK reagent (Calbiochem-Behring Corporation, La Jolla, CA). Creatine kinase control serum was run on each plate (DADE, Division of American Hospital Supply Corporation, Miami, Florida) which was scanned with a model 720 scanning

TABLE 1
Characteristics of Runners

Average	All 15 Runners	BAA-Qualified	AMJA-Registered
Number	15	9	6
Age	36.4	37.5	34.4
Years of Running	5.6	6.4	3.6
Miles per Week	47	78	38
Number of Prior Marathons (12)	4.2	6.8 (9)	3.2 (3)
Best Prior Finishing Time (12)	3:07 (hr:min)	2:53 (hr:min)	3:38 (hr:min)

TABLE 2
Creatine Kinase (U/L)* and Finishing Times for the 15 Participants
(BAA marathon, 1979)

	Pre-Race	Post-Race$_1$	Post-Race$_2$	Finishing Time
1)	135 (U/L)	4750 (U/L)	154 (U/L)	2:35 (hr:min)
2)	259	2739	314	2:51
3)	53	1664	36	2:52
4)	150	8530	187	3:04
5)	167	4050	154	3:04
6)	164	7790	259	3:07
7)	71	1081	136	3:08
8)	149	2841	132	3:11
9)	74	1620	143	3:17
10)	504	9260	144	3:29
11)	62	1694	91	3:37
12)	180	890	218	3:40
13)	93	960	67	3:45
14)	70	319	79	3:59
15)	244	3297	222	4:21

(Normal = <100 U/L)

densitometer (Corning). The normal value for creatine kinase is less than 100 U/L in our laboratory. The standard Student's t-test was used to determine differences between two groups with unequal variances.

RESULTS

Sequential CK values and finishing time for each participant are shown in Table 2. Mean CK values for the entire group and for those finishing before and after three hours and 30 minutes are shown in Table 3. The mean CK for all runners was elevated before the race (161 U/L), peaked 24 hours after competition (3424 U/L), and returned to pre-race levels by four weeks (157 U/L). Creatine kinase drawn within 24 hours after the marathon was significantly higher in the ten runners finishing under 3:30 than in the five slower participants ($p = 0.025$).

Mean CK values before and four weeks after the marathon were also elevated, but were not statistically significant between the faster and slower runners. CK values obtained four weeks after the same race from two elite runners who placed first (2:09:27, a course record) and third (2:12:13) in the race were 296 and 254 U/L, respectively.

TABLE 3
Mean Creatine Kinase Results (U/L) For All Runners and by Finishing Times

Runners	Pre-Race	Post-Race$_1$	Post-Race$_2$
All (15)	161	3424	157
Under 3:30 (10)	173	4433*	166
Over 3:30 (5)	130	1432*	135

*$p = 0.025$

DISCUSSION

Exertional rhabdomyolysis as reported among military recruits has been causally related to inadequate physical conditioning of subjects for the intensity of exertion undertaken [3–5]. The extent of injury is reliably reflected by peaks in creatine kinase in serum, which correlate with serum myoglobin levels [6]. The findings of this study indicate that marathon racing is a sufficient physical stress to provoke substantial if transient rhabdomyolysis in individuals specifically trained for this task.

The inverse relation between the degree of CK elevation 24 hours after the marathon and finishing times of participants is intriguing. It suggests a paradoxically greater degree of transient muscle injury among the faster and presumably more conditioned runners. The risk for development of rhabdomyolysis after the race may depend upon the relationship between overall cardiovascular fitness and the degree of skeletal muscle adaptation to endurance exercise.

Endurance training produces a sequence of biochemical alterations in skeletal muscle which maximizes its capacity for oxidative metabolism [7]. These changes include increased numbers of mitochrondria, higher activities of oxidative respiratory enzymes, and increased capacity to utilize alternate fuels such as ketones and free fatty acids for oxidation. The net effect of these changes is to spare muscle glycogen, which in turn extends the time during which intense exercise can be sustained. The rate of glycogen utilization is dependent upon the intensity of exercise, and increases with physical effort at a higher percentage of maximal oxygen consumption [8]. Endurance training favors a reduced rate of glycogen utilization, which also delays depletion during prolonged exertion.

Glycogen depletion in marathon runners correlates with the phenomenon of "hitting the wall" [9]. Beyond depletion or the wall, oxidative metabolism is almost wholly dependent on ketones and free fatty acids for regeneration of ATP, and insufficient availability of activated phosphates results in decreased efficiency of muscular work. Continued exercise at this stage results in membrane permeability and an efflux of enzymes into serum [10].

Risk for development of rhabdomyolysis during marathon running is dependent upon the relationship between cardiovascular fitness and skeletal muscle oxidative capacity. Runners insufficiently conditioned to sustain a relatively high percentage of maximal oxygen consumption are limited by this exercise parameter, which in turn protects skeletal muscle from sustained maximal stress. Gifted or elite runners, on the other hand, may be protected from rhabdomyolysis less by high aerobic endurance than by skeletal muscle specifically endowed for high aerobic performance. This may in turn relate to percentages of type 2 muscle fibers [11].

The runner at highest risk for development of rhabdomyolysis may fall into an intermediate ability range, where cardiovascular endurance is sufficient for sustained intense effort, but skeletal adaptations to training place limits on efficiency. Compared to more accomplished runners, the time required to complete the marathon distance increases the likelihood of glycogen depletion, after which efficiency falls and pace erodes. Creatine kinase responses to marathon running may vary even for an individual depending upon weather conditions, level of effort expended, and other variables.

Interpretation of CK elevations during training is difficult from these limited data. Elevations of CK before and four weeks after the race might suggest that heavy training produces chronic stress injury, although the high values in two elite runners four weeks after the race suggest that such levels may be a marker for successful

training intensity as well as an index of controlled injury. Sustained, intense training might induce some CK elevation as part of a progressive training effect. This might be accompanied by lesser peaks in total CK after maximal effort such as a marathon race.

Elevations of creatine kinase in serum occur in marathon runners during training and after competition. Levels drawn 24 hours after a marathon race are inversely related to finishing times for runners tested. Further investigations of enzyme responses in runners of varied abilities are required to clarify the relationship between degree of prior conditioning and extent or risk for transient rhabdomyolysis.

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